

REMARKS

Prior to this Amendment, Claims 241-242, 244-245, 248-250, 252-253 and 265-316 were pending. This Amendment adds Claims 317- 370.

Amendment of Claim 249

In the Amendment of June 8, 2008, the language in double brackets was also presented in double brackets, but without a strikethrough of the words. The strikethrough has been added in case there was any doubt that the language should be deleted.

New Claims 317-370

These dependent claims can be divided into six groups, distinguished by the independent claim on which the lowest number of the group depends:

317-328 (317 depends on independent claim 241)

329-335 (329 depends on independent claim 249)

336-347 (336 depends on independent claim 276)

348-354 (348 depends on independent claim 289)

355-358 (365 depends on independent claim 297)

359-362 (359 depends on independent claim 303)

These new claims parallel dependent claims presented prior to this amendment. The highest claim number in each of the six groups of new claims have an extra step, designated as

step (1). Such a step was added by Applicant in response to the conference with the Examiner and Dr. Helms in Serial No. 10/419,462 (on April 22, 2009), and resulted in the allowance of the claims in 10/419,462.

In the present application, however, Applicant have also retained the unamended versions of the claims, as he does not believe that the new step (1) is necessary, and is interested in what legal precedent the Examiner would point to so as to make such an amendment necessary.

New Claims 363-370

These claims specify the type of neoplastic disease as either colon cancer (Claims 363 - 366) or from the group consisting of lung cancer and prostate cancer (Claims 367-370) . Support is found in the specification at pages 57-61 (See for example the two tables and the various Figures referred to).

Objection to Claim 274 (Paragraph 3 of the Office Action)

Responsive to the objection, a period has been added at the end of the claim.

Rejection of Claims 309-316 under 35 U.S.C. 112, first paragraph (Paragraph 5 of the Office Action)

These claims have been rejected on the grounds that they introduce new matter. The Examiner states that the specification at page 18, lines 7-13 provides inadequate support for

Claims 309-316. Applicant understands the rejection to mean that the term “antibody”, not “binding agent”, should be used in the claim. In response, Applicant points to the preceding paragraph in the specification, at page 18, lines 2-6 where it says “.....here ‘epitope’ meaning a target to which a binding agent, *i.e.*, an antibody or a non-antibody binds”. That clarification of the meaning of “epitope for purposes of the present patent application, in combination with the passage at page 18, lines 7-13, provides support for the use of the term “binding agent” in Claims 309-316.

Rejection of Claims 241, 249, 276, 289, 297, 303, and 309 under 35 U.S.C. 112, second paragraph (Paragraph 7a of the Office Action)

The Examiner has rejected claims Claims 241, 249, 276, 289, 297, 303, and 309 as being vague and indefinite because there is no comparison step listed in the claims clarifying what level the individual’s plasma level should be greater than. According to the rejection, it is not clear what plasma level of thrombospondin denotes neoplastic disease and what this level is compared to. The rejection also states that the metes and bounds of the claims cannot be determined. This rejection is traversed on the grounds that follow.

The rejected claims state that, the greater the plasma level (of a thrombospondin fragment or fragments), the more likely that the diagnosis will be that a neoplastic disease is present in the individual. The comparison step is inherent in the language of the claim. The phrase “greater than” implies a comparison. In the case of dependent Claims 242 and 244 for example, it is clarified that the comparison can be between two individuals (one considered not to have

neoplastic disease) or the same individual at successive time points. (Similar pairs of dependent claims are 250/252, 277/278, 290/291, 298/299, and 304/305.) In each case, the higher plasma level of fragment or fragment(s) indicates a higher likelihood that neoplastic disease is present.

Rejection of Claims 276 and 312 under 35 U.S.C. 112, second paragraph (Paragraph 7b of the Office Action)

These two claims are rejected on the grounds that they recite amino acid residues and corresponding position numbers, but there are no sequences or SEQ ID number information provided.

In response, Applicant has amended Claims 276 and 312 to specify SEQ ID No. 38 and where the amino acid residues are referred to therein. SEQ ID No. 38 is set forth in the application at page 42, lines 19 - 40 (and in the Sequence Listing for this case), and as being the amino acid sequence of human thrombospondin-1 (See application at page 42, line 15.)

The amino acid numbers that appeared in Claims 276 and 312 prior to this amendment were 165, 263, 792, and 982, corresponding to the numerical portions of I-165, V-263, R-792 and Y-982, respectively. (The letters, I, V, R, and Y correspond to the one-letter amino acid abbreviations; see Specification at page 13, lines 25-26). The numbers 165, 263, 792 and 982 were based on “mature thrombospondin”; i.e. thrombospondin in which the 18-amino acid signal peptide had been removed. (See, application at page 43, lines 2-5). The size of the signal peptide could be as small as 18 amino acids or as large as 22 amino acids. (Application at page 43, lines 2-5). In the present application it is assumed to be 18 amino acids in length.

The numbers 183, 281, 810, and 1000, added to the claims via the present amendment are in each case a value of 18 more than their corresponding number prior to this amendment. These new numbers refer to residue numbers in the full thrombospondin sequence (SEQ ID NO:38) from which the 18-amino acid signal peptide had not been removed.

Rejection of Claim 309 under 35 U.S.C. 112, second paragraph (Paragraph 7c of the Office Action)

Claim 309 is rejected on the grounds that, in lines 3 and 4, it recites “utilizing a first binding agent to obtain a quantitation of a total, thrombospondin plus either the thrombospondin fragment or fragments” and that it is not clear (a) what product or molecule has been quantitated and (b) what product or molecule the term “total” describes. Applicant responds as follows:

Claim 309 is based on the presence of an epitope (or epitopes) present in the fragments and/or thrombospondin and furthermore on the binding of agents (such as an antibody) to such epitopes (see the Specification at page 18, lines 7-13, which section was referred to in the rejection of Paragraph 5 of the Office Action.) Quantitations based on such assays provide measures of the numbers of molecules. (The reaction of the agent to the epitope is “blind” to the size of the molecule it binds to, and therefore the mass of the molecule it is binding to.) Accordingly “total” refers to the sum of two numbers, each of which is a measure of a number of molecules.

**Rejection of Claims 241, 245 248, 249, 253, 256 and 265-276 under 35 U.S.C. 102(b) as
being anticipated by Jackowski et al./ U.S. Patent Application number 2003/0119074
(Paragraph 9 of the Office Action)**

This rejection is traversed on the grounds that Jackowski does not disclose an assay directed at the diagnosis of neoplastic disease, as specified in Applicant's claims. Rather Jackowski's disclosure is directed at Alzheimer's Disease. Should the Examiner believe that such a distinction is not sufficient to overcome the rejection, Applicant respectfully requests that the Examiner indicate what judicial opinion the rejection is based on.

**Rejection of Claims 241, 242, 244, 245 248-250, 252, 253, 256 and 256-316 under 35 U.S.C.
102(e) as being anticipated by U.S. Patent Application number 2003/0166017 (McCarthy)
(Paragraph 10 of the Office Action)**

This rejection is traversed on the grounds that McCarthy does not disclose an assay directed at the diagnosis of neoplastic disease, as specified in Applicant's claims. Rather McCarthy's disclosure is directed at cardiovascular disease . Should the Examiner believe that such a distinction is not sufficient to overcome the rejection, Applicant respectfully requests that the Examiner indicate what judicial opinion the rejection is based on.

**Rejection of Claims 241, 242, 245 248-250 , 252, 253, 256 and 256-316276 under 35 U.S.C.
102(e) as being anticipated by U.S. Patent Application number 2003/0166017 (McCarthy)**

(Paragraph 12 of the Office Action)

This rejection is traversed on the grounds that neither WO 98/07035 nor McCarthy discloses an assay directed at the diagnosis of neoplastic disease, as specified in Applicant's claims. Rather the WO98/07035 disclosure is directed at arthritis and McCarthy's disclosure is directed at cardiovascular disease. Should the Examiner believe that such a distinction is not sufficient to overcome the rejection, Applicant respectfully requests that the Examiner indicate what judicial opinion the rejection is based on.

Provisional rejection of claims as being unpatentable over claims of copending application No. 10/419,462 on the grounds of nonstatutory obviousness-type double patenting

(Paragraph 14 of the Office Action)

Applicant notes that a continuation application (Serial No. 12/543,855) of application serial number 10/419,462 was filed on August 19, 2009.

Applicant notes that he has filed a terminal disclaimer in serial number 10/419,462 relating to that application and the present application.

Applicant believes that it is premature to sign a terminal disclaimer in the present case since there are no allowed claims in the present application.

Provisional rejection of claims as being unpatentable over claims of copending application No. 10/525,610 on the grounds of nonstatutory obviousness-type double patenting

(Paragraph 15 of the Office Action)

Application ser. no. 10/782,698
Attorney Docket No. W1107/20009
Amendment Dated September 3, 2008

Applicant believes that it is premature to sign a terminal disclaimer in the present case since there are no allowed claims in the present application.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for initial examination and allowance, the Examiner is invited to phone Applicants' undersigned attorney at **610-724-2952**.

Respectfully submitted,

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